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Lippuner, K ; Grifone, S ; Schwenkglenks, M ; Schwab, P ; Popp, A W ; Senn, C ; Perrelet, R

Abstract: In Switzerland, the number, incidence, and cost of acute hospitalizations for major osteoporotic fractures (MOF) and major cardiovascular events (MCE) increased in both women and men between 2000 and 2008, although the mean length of stay (LOS) was significantly reduced. Similar trend patterns were observed for hip fractures and strokes (decrease) and nonhip fractures and acute myocardial infarctions (increase). INTRODUCTION: The purpose of this study was to compare the trends and epidemiological characteristics of hospitalizations for MOF and other frequent diseases between years 2000 and 2008 in Switzerland. METHODS: Trends in the number, age-standardized incidence, mean LOS, and cost of hospitalized MOF and MCE (acute myocardial infarction, stroke, and heart failure) were compared in women and men aged 45 years, based on data from the Swiss Federal Statistical Office. RESULTS: Between 2000 and 2008, the incidence of acute hospitalizations for MOF increased by 3.4% in women and 0.3% in men. In both sexes, a significant decrease in hip fractures (-15.0% and -11.0%) was compensated by a concomitant, significant increase in nonhip fractures (+24.8% and +13.8%). Similarly, the incidence of acute hospitalizations for MCE increased by 4.4% in women and 8.2% in men, as an aggregated result from significantly increasing acute myocardial infarctions and significantly decreasing strokes. While the mean LOS in the acute inpatient setting decreased almost linearly between years 2000 and 2008 in all indications, the inpatient costs increased significantly ($p < 0.001$) for MOF (+30.1% and +42.7%) and MCE (+22.6% and +47.1%) in women and men, respectively. CONCLUSIONS: Between years 2000 and 2008, the burden of hospitalized osteoporotic fractures to the Swiss healthcare system has continued to increase in both sexes. In women, this burden was significantly higher than that of MCE and the gap widened over time.

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Comparative trends in hospitalizations for osteoporotic fractures and other frequent diseases between 2000 and 2008

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Mini-Abstract

In Switzerland, the number, incidence, and cost of acute hospitalizations for major osteoporotic fractures and major cardiovascular events increased in both women and men between 2000 and 2008, although the mean length of stay was significantly reduced. Similar trend patterns were observed for hip fractures and strokes (decrease) and non-hip fractures and acute myocardial infarctions (increase).

Abstract

Purpose : To compare the trends and epidemiological characteristics of hospitalizations for major osteoporotic fractures (MOF) and other frequent diseases between year 2000 and 2008 in Switzerland.

Methods : Trends in the number, age-standardized incidence, mean length of stay and cost of hospitalized MOF (hip, clinical spine, distal radius, and proximal humerus), major cardiovascular events (MCE: acute myocardial infarction, stroke, heart failure), chronic obstructive pulmonary disease (COPD), and breast carcinoma were compared in women and men aged ≥45 years, based on data from the Swiss Federal Statistical Office hospital database and population statistics.

Results : Between 2000 and 2008, the age-standardized incidence of acute hospitalizations for MOF increased by 3.4% in women and 0.3% in men. In both sexes, a significant decrease in hip fractures (-15.0% and -11.0%) was compensated by a concomitant, significant increase in non-hip fractures (+24.8% and +13.8%). Similarly, the incidence of acute hospitalizations for MCE increased by 4.4% in women and 8.2% in men, as an aggregated result from significantly increasing acute myocardial infarctions and significantly decreasing strokes. While the mean length of stay in the acute inpatient setting decreased almost linearly between year 2000 and

2008 in all indications, the inpatient costs increased significantly ($p<0.001$) for MOF (+30.1%, +42.7%) and MCE (+22.6%, +47.1%) in women and men, respectively. In women in 2008, the cost of acute hospitalizations was more than threefold higher for MOF than for COPD and breast cancer and 1.5 fold higher than for any MCE. In men it was comparable to that of COPD, acute myocardial infarction, and heart failure.

Conclusions : In conclusion, between year 2000 and 2008, the burden of hospitalized osteoporotic fractures to the Swiss healthcare system has continued to increase in both sexes. In women, this burden was significantly higher than that of major cardiovascular events and the gap between both disease groups widened over time.

Key words

osteoporosis, hip fracture, clinical spine fracture, distal radius fracture, proximal humerus fracture, acute myocardial infarction, stroke, heart failure, chronic obstructive pulmonary disease, breast cancer, epidemiology, cost, Switzerland.

Introduction

Osteoporotic fractures are one of the leading causes of morbidity and mortality in industrialized countries [1]. While virtually any fracture may result as a complication from underlying osteoporosis, “typical” osteoporotic fractures occur at the hip, spine, distal forearm, and proximal humerus. Together, they are traditionally referred to as major osteoporotic fractures (MOF) [1-3].

In year 2000, in all women living in Switzerland, the overall incidence of hospitalizations for any osteoporotic fracture was twice as high as that for breast cancer and pooled major cardiovascular events (MCE: acute myocardial infarction, stroke, and heart failure), and almost three times that of chronic obstructive pulmonary disease (COPD) [4]. In Swiss men, the overall incidence of hospitalizations for any osteoporotic fracture was half that of pooled MCE and two thirds of that of COPD [4]. As recently published, the age-standardized incidences of hospitalized MOF continued to increase in Swiss women and men aged 45 years and older between the year 2000 and 2007, driven by an increasing number and incidence of hospitalizations for non-hip fractures although the number of hip fractures was on the decline [5].

The aim of the present analysis was to compare the trends and epidemiological characteristics, in female and male patients aged 45 years or older, of major osteoporotic fractures, major cardiovascular events, COPD, and breast carcinoma (women only) in Switzerland, between the years 2000 and 2008. Predefined parameters of interest were: absolute number and incidence of hospitalizations, number of hospital days due to fractures, and cost of hospitalizations.

Methods

A summary of the data processing flow and relevant data sources is shown in **Figure 1**.

Selected ICD-10 codes

Diseases were selected according to the 10th Edition of the International Classification of Diseases (ICD-10) issued by the World Health Organization [6]. Major osteoporotic fractures were divided into two categories: hip (ICD-10 codes S72.0 (fracture of the femoral neck), S72.1 (pertrochanteric fracture), and S72.2 (subtrochanteric fracture)) and non-hip. Non-hip fractures were defined as: spine fractures coded S22.0 (fracture of the thoracic spine), S22.1 (multiple fractures of the thoracic spine), S32.0 (fracture of the lumbar spine), S32.7 (multiple fractures of the lumbar spine), and S32.8 (other fractures of the lumbar spine); fractures of the distal forearm coded as S52.5 (fracture of the distal radius) and S52.6 (combined fracture of the distal radius/ulna); fractures of the proximal humerus coded as S42.2 (fracture of the proximal humerus).

Major cardiovascular events were defined as myocardial infarction coded I21 (acute myocardial infarction) and I22 (subsequent myocardial infarction); stroke coded I63 (cerebral infarction), I64 (stroke, not specified as haemorrhage or infarction), I65 (occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction), and I66 (occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction); heart failure coded I50 (heart failure). Chronic obstructive pulmonary diseases were defined as codes J40 (bronchitis, not specified as acute or chronic), J41 (simple and mucopurulent chronic bronchitis), J42 (unspecified chronic bronchitis), J43 (emphysema), J44 (other chronic obstructive pulmonary disease),

J45 (asthma), J46 (status asthmaticus), and J47 (bronchiectasis). Breast carcinoma corresponded to the ICD-10 code C50 (malignant neoplasm of breast).

Source of hospital statistics

The administrative and medical statistics database of the Swiss Federal Statistical Office (SFSO) was used. All Swiss acute care hospitals, rehabilitation centers and specialized clinics, are obliged to supply their medical data to the SFSO (age, sex, number of hospitalizations coded according to the ICD-10 requirements, and duration of hospitalization). Data collection is coordinated by the SFSO. Data consistency and quality is ensured at the individual hospital, cantonal, and federal level through the mandatory use of a plausibility testing software developed by the SFSO [7]. This software performs more than 700 plausibility checks on single and pooled variables, including multiple interdependent variable testing and diagnostic code vs. treatment code testing). Inconsistencies and errors indicated in the log files are corrected at the appropriate level (individual hospital for source data, canton for inconsistencies across hospitals, and confederation for inconsistencies across cantons) following a feedback loop. This process ensures low error rates so that the level of plausibility of the reported diagnostic codes exceeds 95% [8]. Only medical data from Swiss acute hospital settings were retained for the present analysis. Data from rehabilitation centers and specialized clinics were excluded to prevent double counting. The degree of completeness for all records for years 2000 to 2008 was: 81.2%, 84.9%, 95.0%, 94.1%, 96.2%, 98.2%, 98.5%, 98.6%, and 98.8%.

Raw data for the number of hospitalizations for the selected ICD-10 codes and corresponding duration of hospitalization, were obtained for women and men aged ≥45 years. Only the primary diagnostic code, i.e. the reason for hospitalization, was

considered for each patient to prevent double counting. All raw data were extrapolated pro-rata to 100% to compensate for incomplete coverage and to become representative for Switzerland as a whole.
Data on the Swiss population structure between 2000 and 2008, split by 10-year age groups and sex, was also obtained from the SFSO.

Epidemiological characteristics of hospitalizations

The age-standardized incidence of hospitalizations, the number of patient-days spent in hospital and the mean length of hospital stay (LOS) per patient were calculated by 10-year age groups starting from age 45 onwards and by sex, for all selected ICD-10 codes grouped into the categories defined above. Annual crude incidences and 95% confidence intervals per 100'000 persons in years 2000 to 2008 were calculated by sex and 10-year age groups starting from age 45 onwards. Annual age-standardized incidences per 100'000 persons and 95% confidence intervals were calculated by sex based on 10-year age groups and adjusted for the age structure of the Swiss population in year 2000 according to a method published earlier [9]. Standardized incidence rate ratios and 95% confidence intervals were calculated to assess the change in incidence over time. As the goodness-of-fit of tentative Poisson regression models could not be confirmed, related time trends were assessed by fitting gender-specific negative binomial models with ICD-10 code and year as covariates.
The mean length of hospital stay was estimated by dividing the total number of patient-days spent in hospital by the number of hospitalizations. The cost of hospitalizations was estimated by multiplying the number of patient-days spent in hospital by the yearly average cost of one day in-hospital in Swiss Francs (CHF) between 2000 and 2008. The latter was obtained from yearly summary tables derived

from the hospital statistics database of the SFSO for each year of analysis and was not inflation adjusted [10]. The effects of time on mean length of stay and hospitalization cost was tested for statistical significance by the two-way ANOVA method. All calculations were done with the statistical software StatsDirect version 2.7.8 (StatsDirect Ltd, Altrincham, Cheshire, UK). Negative binomial regression was performed in Stata/MP version 11.1 (Stata Corporation, College Station, Texas, USA).

Results

Swiss population structure

Between year 2000 and 2008, the number of women and men aged 45 years and older increased by 13.3 and 17.4%, respectively.

Number of hospitalizations (Figure 2)

Between 2000 and 2008, the absolute number of acute care hospitalizations for major osteoporotic fractures in patients aged ≥45 years increased from 13'948 to 16'339 (+17.1%) in women and from 4'670 to 5'634 (+20.6%) in men, essentially driven by non-hip fractures (+41.3% and +34.6%, respectively). During the same time, the number of hip fractures decreased from 7'684 to 7'485 (-2.6%) in women and remained stable in men (from 2'538 to 2'765, +1%) in men. Similarly, the number of hospitalizations for major cardiovascular events increased from 9'530 to 11'271 (+18.3%) and from 12'634 to 16'378 (+29.6%) in women and men, respectively. In contrast, the number of hospitalizations for COPD decreased from 5'115 to 4'210 (-17.7%) and from 6'844 to 4'934 (-27.9%) in women and men, respectively. Finally the number of hospitalizations for breast cancer decreased from 9'400 to 7'650 (-18.6%) in women.

Age-standardized incidence of hospitalizations

In women, as shown in **table 1A**, the age-standardized incidence of hospitalized MOF increased by 3.4% between 2000 and 2008 (p for trend, 0.121), the significant decrease in hip fractures (-15.0%; p for trend, < 0.001) being fully compensated by a concomitant significant increase in hospitalized non-hip fractures (+24.8%; p for trend, 0.002). The latter resulted from an increase in hospitalized fractures of the

spine (+32.2%; p for trend, 0.008), the distal radius (+31.8%; p for trend, 0.005), and the proximal humerus (+10.3%, p for trend, 0.141). Similarly, the incidence of acute hospitalizations for major cardiovascular events increased by 4.4% (p for trend, 0.558) during the observation period, as an aggregated result of a significant increase in acute myocardial infarctions (+29.5%; p for trend, 0.016) opposed by a significant decrease in hospitalized strokes (-17.8%; p for trend, 0.016), and with no change in the incidence of hospitalizations for heart failure (+0.8%; p for trend, 0.926). Finally, the incidence of hospitalizations for COPD and breast cancer decreased significantly by 27.3% (p for trend, 0.016) and 28.2% (p for trend, < 0.001), respectively.

In men, as shown in **table 1B**, the incidence of hospitalized MOF did not change between 2000 and 2008 (+0.3%; p for trend, 0.918). The significant reduction in incident hip fractures (-11.0%; p for trend, 0.031) was totally offset by a significant increase in non-hip fractures (+13.8%; p for trend, 0.032), mainly driven by fractures of the distal radius (+29.2%; p for trend, < 0.001) and the proximal humerus (+12.5%; p for trend, 0.295). The incidence of acute hospitalizations for major cardiovascular events increased significantly by 8.2% (p for trend, 0.019). Interestingly, this overall increase resulted from an increase in hospitalizations for myocardial infarctions (+24.7%; p for trend, < 0.001) and heart failure (+8.5%; p for trend, 0.208) opposed by a significant reduction in the incidence of stroke (-28.1%; p for trend, 0.006). Finally, incident hospitalizations for COPD were significantly reduced by 39.7% (p for trend, 0.002).

The overall pattern of changes in age-standardized incidences was consistent across sexes: decreasing incidences of hospitalizations for hip fractures and stroke, increasing incidences in hospitalizations for non-hip major osteoporotic fractures and

acute myocardial infarctions, decreasing incidence in hospitalizations for COPD. The observed increasing or decreasing trends in any disease category went in the same direction and were of similar magnitude in all age groups (figure 3).

Patient-days in hospital and mean length of stay

The total number of days spent during the acute hospitalization phase decreased almost linearly between year 2000 and 2008 in all indications of interest and in both sexes. In women, the highest relative decrease was observed for COPD (from 89'554 to 56'099 days, -37.4%), followed by breast carcinoma (from 90'951 to 57'842days, -36.4%), major cardiovascular events (from 164'685 to 124'384 days, -24.5%), and major osteoporotic fractures (from 224'244 to 179'461, -19.9%). Therefore, hospitalization for MOF remains a major contributor of days spent in hospital by women aged 45 years or more, responsible of 3 times more days of hospitalization than COPD and breast cancer, and 1.5 times more days than any major cardiovascular event.

In men, the highest relative decrease in days spent in hospital was observed for COPD (from 107'329 to 60'663, -43.5%) followed by major osteoporotic fractures (from 71'477 to 62'828, -12.1%), and major cardiovascular events (from 174'858 to 158'441, -9.4%). Therefore, in 2008, there were as many days spent in hospital by men for COPD, acute myocardial infarction (67'997 days), and heart failure (57'822 days) as for major osteoporotic fractures.

These considerable reductions in total days spent in hospital for all indications of interest were essentially due to a relevant and statistically significant reduction of the mean length of stay (LOS) as shown in **table 2**.

Cost of hospitalizations

As described above, the mean LOS for patients hospitalized because of fractures decreased substantially between 2000 and 2008. The effect of this was counterbalanced, however, by rising hospital costs: the mean cost per day of hospitalization increased from CHF 996.00 to CHF 1,618.00, over the same period, a rise of 62%. The effects on hospitalization costs by selected diagnostic codes are shown in **figure 4.**

In women, hospitalization cost for major osteoporotic fractures increased from CHF 223 mio to 291 mio (+30.1%, $p<0.001$ for time trend) and from 164 to 201 mio (+22.6%, $p<0.001$) for major cardiovascular events. The cost of hospitalizations for COPD and breast cancer remained almost unchanged (from CHF 89 to 91 mio, +1.7%, $p= 0.168$ and from 91 to 94 mio, +3.3%, $p=0.003$, respectively). Overall, in women in 2008, the cost of acute hospitalizations was more than threefold higher for major osteoporotic fractures than for COPD and breast cancer and 1.5 fold higher than for any major cardiovascular event. As shown in figure 5, osteoporotic fractures contributed to approximately 60% of the total costs of MOF and MCE in women.

In men, the cost of acute hospitalizations for major osteoporotic fractures and major cardiovascular events between 2000 and 2008 increased by 42.7% (from CHF 71 to 102 mio, $p<0.001$ for time trend) and by 47.1% (from CHF 174 to 256 mio, $p<0.001$), respectively. Therewhile, the cost of hospitalizations for COPD was reduced by 8.2% (from CHF 107 to 98 mio, $p=0.078$). Overall, in men in 2008, the cost of acute hospitalizations for MOF was comparable to that of COPD, acute myocardial infarction (CHF 110 mio), and heart failure (CHF 94 mio). As shown in figure 5, osteoporotic fractures represented approximately 30% of the total costs of MOF and MCE in men.

Discussion

The present analysis reports the epidemiological characteristics of hospitalizations in the acute care setting of patients with major osteoporotic fractures, major cardiovascular events, chronic obstructive pulmonary disease, or breast carcinoma in Switzerland between year 2000 and 2008. For the first time, time trends were established by using a nationwide database of medical records following an identical methodology, which ensures highest possible homogeneity in results and should allow for comparisons with only little potential for bias. In this analysis, the age-standardized rates of hospitalizations for MOF and MCE increased during the observation period, driven by an increase in non-hip fractures and acute myocardial infarctions, respectively. In addition, the mean length of hospital stay decreased significantly in all indications of interest, the cost effect of which was offset by the increase in cost per day of hospitalization. Overall, the total cost of hospitalizations, which aggregates the cost effect of the number of hospitalizations, mean length of hospital stay, and cost per day of hospitalization, increased by 30% and 43% for MOF and 23 and 47% for MCE in women and men, respectively. The total cost incurred by hospitalizations for COPD and breast cancer remained virtually unchanged. During the same time, hospitalizations for hip fractures, stroke, COPD, and breast cancer decreased significantly. Reported changes followed similar patterns in both sexes, although of different orders of magnitude.

In Swiss women, during the 9 years of observation, osteoporosis and its complications, as measured by the characteristics of hospitalizations for major osteoporotic fractures, remained a key contributor to the economic burden of healthcare. As confirmed by the present analysis, hip fractures seem on the decline in Swiss women which confirms earlier findings from our group [5] and others [11,

12]. This possible reversal of a secular trend is consistent with reports from other countries such as USA [13-15], Canada [16, 17], Japan [18], Finland [19], and Denmark [20]. Similar observations were made in neighbour countries such as France [21] and Austria [22] but not in Italy [23] and Germany [24, 25]. In contrast, the incidence of hospitalizations for non-hip fractures steadily increased between year 2000 and 2008 in Swiss women. This effect was observed for all localizations of non-hip fractures (spine, distal radius, and proximal humerus). Possible explanations will remain speculative and were detailed elsewhere [5]. We are not aware of other publications confirming or infirming this observation with the exception of earlier reports from Finland which indicated that low-trauma knee [26], ankle [27], and distal humeral [28] fractures may be stabilizing or even declining in this country. Importantly, the present analysis reports hospitalized fractures only. Whether the total incidence of hospitalized and non-hospitalized non-hip fractures has increased cannot be concluded from the present data. However, as ongoing health care reform efforts have led to a global shift from inpatient to outpatient care [29], the matter deserves further investigation. The age-standardized incidence of hospitalizations for hip and non-hip fractures in men followed a similar pattern as in women but with a lower magnitude of change.

Interestingly, in women, the incidence of hospitalizations for acute myocardial infarctions increased strongly while they stagnated for heart failure and decreased for stroke with a similar pattern in men. Although a milestone regarding the characteristics of acute coronary syndromes in the real world was achieved already in 1997 by launching the AMIS (Acute Myocardial Infarction in Switzerland) and AMIS Plus registry [30], we are not aware of previously published trend patterns for hospitalized major cardiovascular events in Switzerland. An increasing number of

publications reports the association between cardiovascular diseases and osteoporotic fractures. Among the very first indices in this regard, a Swedish registry collected 273'288 strokes and 24'666 fractures, of which 14'263 hip fractures, between 1987 and 1996 and concluded that after a hospitalization for stroke, there was a more than 7-fold increase in fracture risk during the first year after hospitalization for stroke [31]. In 2007, Sennerby et al showed that women with cardiovascular disease had a substantially increased risk of hip fracture, suggesting possible common pathologic pathways for osteoporotic fractures and cardiovascular diseases [32]. In addition, in a cohort of 31'936 Swedish twins born in 1914-1944 followed up from the age of 50 years, the same authors reported that a diagnosis of cardiovascular disease was significantly associated with risk of subsequent hip fracture within the same individual and in his or her co-twin without index diagnosis [33]. In the present analysis, we report an increasing incidence of both major osteoporotic fractures and major cardiovascular diseases between 2000 and 2008 in Switzerland, which is consistent with a possible association between both disease entities. We also report decreasing trends in hip fractures and stroke and increasing trends in non-hip fractures and acute myocardial infarctions, which raises the question whether the supposed association between osteoporosis and cardiovascular diseases might be more multifaceted than suggested to date.

The present analysis based on data of the medical database of the SFSO did not allow for identification of potential underlying associations or causes for the reported time trends. The earlier mentioned prospective AMIS Plus registry collects 230 variables of patients hospitalized for acute coronary syndromes in 76 Swiss hospitals participating on a voluntary basis. If a similar registry existed for osteoporotic fractures, ideally in the same or a subset of the AMIS hospitals, database linkages

could offer a unique opportunity for exploring further the associations between fractures and cardiovascular diseases. Furthermore, both fractures and major cardiovascular events often lead to patient discharge to a rehabilitation center. Here again, a fracture registry combined with AMIS Plus could possibly contribute to identify common prognostic factors and to improve outcomes.

The present analysis reports hospitalized clinical events only. It is well known that many osteoporotic fractures are treated in the outpatient setting. Based on data from the Swiss nationwide survey in the OsteoCare cohort, which included 3667 consecutive women and men aged 50 years and older and presenting to the emergency ward of participating hospitals with a fragility fracture [34], virtually all hip fractures, approximately half of proximal humerus fractures, one third of distal radius fractures, and one fourth of clinical spine fractures were hospitalized in Switzerland [3]. These observations are broadly consistent with reports from other countries [35]. On the other hand, as many as 25% of all coronary events are lethal before the patient reaches the hospital, a proportion that continues to increase as a result of the decline in in-hospital deaths observed during the past decades [36]. Therefore, the proposed comparisons across diseases should be considered as restricted to hospitalizations only.

We reported on major osteoporotic fractures, i.e. of a subset of all hospitalized osteoporotic fractures. Achieving completeness would have required the very cumbersome use of osteoporosis attribution rates, as was exemplified earlier [4, 37]. Using the present approach, major osteoporotic fractures were estimated to represent only 77 and 72% of attributable fractures in women and men in year 2000, respectively [3-5]. Therefore, absolute numbers, incidences, hospital days and related costs reported in the analysis should be considered conservative. Data

completeness was 81.2% and 84.9% in years 2000 and 2001, respectively, and exceeded 95.0% thereafter. The extrapolation to 100% could have induced a selection bias when comparing year 2008 with 2000. However, the trends observed over the 9 years were consistent year over year in all diseases of interest and no outliers were identified.

Of note, the total cost estimate for osteoporotic fractures (CHF 393 mio) reported in the present analysis refers to direct medical costs of acute hospitalizations for MOFs only. The total direct medical cost of all hospitalized osteoporotic fractures can be extrapolated to CHF 524 mio, to which the inpatient rehabilitation and nursing home costs should be added. These represent approximately 50% of the total cost of the inpatient management of osteoporotic fractures, as already published earlier by our group [38], so that the total cost of treating hospitalized osteoporotic fractures in Switzerland exceeded CHF 1 billion in 2008. Cost estimates calculated in the present analysis are based on the nationwide average real cost per day of hospitalization and not on discipline-specific costs or Diagnosis Related Groups (DRGs). Therefore, cost estimates should be regarded as approximations, until the introduction of the DRG system will allow more precise estimates.

Finally, we did not attempt a projection based on observed trends. According to demographic scenarios from the SFSO, the Swiss population older than 65 years of age will almost have doubled in 2050 [39]. Therefore, assuming the current time trends remaining unchanged, the declining incidence of hip fractures and strokes will not be sufficient to reduce the absolute number of hospitalizations for these diseases in the coming decades. A representative cohort or a fracture registry linked to the AMIS Plus registry would contribute to better anticipation of future trends and allow

for monitoring the effects of public health measures aimed at reducing fracture and cardiovascular risk.

In conclusion, between year 2000 and 2008, the burden of hospitalized osteoporotic fractures to the Swiss healthcare system has continued to increase in both sexes. In women, this burden was significantly higher than that of major cardiovascular events and the gap between both disease groups widened over time. More research is warranted to better understand the causal drivers behind these trends.

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Conflicts of interest

None.

Tables and figures

Figure legends

Figure 1: Data sources and data processing flow. SFSO = Swiss Federal Statistical Office; ICD = International Classification of Diseases; COPD = Chronic Obstructive Pulmonary Diseases.

Figure 2: Number of acute care hospitalizations in women (A) and men (B) for selected diseases between year 2000 and 2008

Figure 3: Age-standardized incidence of hospitalizations per 100’000 in women (A) and men (B) aged 45 years or more by 10-year age groups

Figure 4: Cost of acute hospitalizations in women (A) and men (B) aged 45 years and older (mio. CHF)

Figure 5: relative cost contribution of major osteoporotic fractures and major cardiovascular events in women (A) and men (B) aged 45 years and older between year 2000 and 2008.

Table 1: age-standardized incidence of hospitalizations per 100'000 women (A) and men (B) aged 45 years or more (95% confidence interval)

Table 1A

	2000	2001	2002	2003	2004	2005	2006	2007	2008	Incidence rate ratio 2008 vs 2000 (95% CI)
Major osteoporotic fractures	**901**	**976**	**955**	**965**	**942**	**942**	**964**	**933**	**925**	**1.03**
	(886-916)	(961-992)	(940-970)	(950-980)	(928-957)	(927-956)	(949-978)	(919-948)	(911-939)	(1.00-1.05)
Hip fractures	496	535	500	488	460	439	435	433	421	0.85
	(485-507)	(524-546)	(489-511)	(478-499)	(450-471)	(429-449)	(425-445)	(423-443)	(411-430)	(0.82-0.87)
Non-hip fractures	405	441	455	477	482	503	529	500	504	1.25
	(395-415)	(431-452)	(444-465)	(466-488)	(471-493)	(492-513)	(518-540)	(490-511)	(494-515)	(1.21-1.29)
Spine fractures	*84*	*93*	*93*	*95*	*91*	*95*	*97*	*107*	*110*	*1.32*
	(79-88)	*(88-97)*	*(88-98)*	*(90-100)*	*(86-95)*	*(90-98)*	*(92-102)*	*(102-112)*	*(105-115)*	*(1.23-1.41)*
Distal radius fractures	*187*	*207*	*216*	*240*	*236*	*263*	*276*	*246*	*246*	*1.32*
	(180-194)	*(200-214)*	*(209-223)*	*(233-248)*	*(299-244)*	*(255-271)*	*(268-284)*	*(238-253)*	*(239-254)*	*(1.26-1.38)*
Proximal humerus fractures	*134*	*141*	*145*	*141*	*155*	*145*	*156*	*148*	*148*	*1.10*
	(128-140)	*(135-147)*	*(139-151)*	*(136-147)*	*(149-161)*	*(139-150)*	*(150-161)*	*(142-154)*	*(142-153)*	*(1.04-1.17)*
Major CV events	**615**	**622**	**558**	**539**	**525**	**514**	**564**	**577**	**639**	**1.04**
	(603-628)	(610-634)	(546-569)	(527-550)	(514-536)	(503-525)	(552-575)	(565-590)	(627-651)	(1.01-1.07)
Acute myocardial infarction	190	202	188	183	177	179	200	211	246	1.29
	(183-197)	(195-209)	(181-194)	(176-189)	(170-183)	(173-186)	(193-206)	(204-218)	(239-254)	(1.23-1.36)
Stroke	175	175	140	138	132	123	128	121	143	0.82
	(169-182)	(168-181)	(134-146)	(132-144)	(127-138)	(118-128)	(123-133)	(116-126)	(138-149)	(0.78-0.86)
Heart failure	250	245	230	218	215	211	236	245	249	1.00
	(242-258)	(237-253)	(223-237)	(211-225)	(208-222)	(205-218)	(229-243)	(238-252)	(242-257)	(0.96-1.04)
COPD	**330**	**295**	**279**	**265**	**252**	**256**	**241**	**268**	**241**	**0.73**
	(321-339)	(286-303)	(271-287)	(257-273)	(244-260)	(248-263)	(234-249)	(261-276)	(234-248)	(0.70-0.76)
Breast carcinoma	**607**	**612**	**535**	**546**	**493**	**470**	**453**	**428**	**438**	**0.72**
	(595-619)	(600-624)	(523-546)	(535-557)	(483-504)	(459-480)	(443-463)	(419-438)	(428-447)	(0.70-0.74)

Table 1B

	2000	2001	2002	2003	2004	2005	2006	2007	2008	Incidence rate ratio 2008 vs 2000 (95% CI)
Major osteoporotic fractures	**351**	**375**	**351**	**366**	**354**	**356**	**362**	**360**	**352**	**1.00**
	(341-361)	(364-385)	(341-361)	(353-373)	(344-364)	(347-366)	(353-372)	(350-369)	(343-361)	(0.96-1.04)
Hip fractures	191	197	186	182	174	164	176	166	170	0.89
	(183-198)	(189-204)	(179-193)	(175-189)	(168-181)	(158-171)	(164-178)	(160-172)	(163-176)	(0.84-0.94)
Non-hip fractures	160	178	165	181	180	192	191	194	182	1.14
	(153-167)	*(171-185)*	*(158-171)*	*(174-188)*	*(173-187)*	*(185-199)*	*(184-198)*	*(187-201)*	*(175-189)*	(1.07-1.20)
Spine fractures	*64*	*67*	*60*	*66*	*67*	*65*	*67*	*74*	*67*	*1.04*
	(60-68)	*(63-72)*	*(56-64)*	*(62-70)*	*(63-71)*	*(61-69)*	*(63-71)*	*(70-79)*	*(63-71)*	*(0.95-1.14)*
Distal radius fractures	*48*	*53*	*55*	*61*	*58*	*64*	*68*	*63*	*62*	*1.29*
	(44-51)	*(49-57)*	*(51-58)*	*(57-65)*	*(54-62)*	*(60-68)*	*(63-72)*	*(59-67)*	*(58-66)*	*(1.17-1.43)*
Proximal humerus fractures	*48*	*57*	*51*	*54*	*55*	*63*	*57*	*57*	*54*	*1.11*
	(45-52)	*(53-61)*	*(47-54)*	*(50-58)*	*(51-59)*	*(59-67)*	*(53-61)*	*(53-60)*	*(50-57)*	*(1.00-1.23)*
Major cardiovascular events	**949**	**972**	**896**	**873**	**865**	**864**	**984**	**1'009**	**1'027**	**1.08**
	(932-965)	(956-989)	(880-912)	(857-888)	(850-880)	(850-879)	(969-1000)	993-1024)	(1011-1042)	(1.06-1.11)
Acute myocardial infarction	458	463	449	435	429	438	510	535	571	1.25
	(446-469)	(452-474)	(438-460)	(424-445)	(419-440)	(427-448)	(498-521)	(523-546)	(560-583)	(1.21-1.29)
Stroke	210	203	176	177	173	161	167	153	151	0.72
	(202-217)	(195-210)	(169-183)	(170-184)	(167-180)	(155-168)	(160-173)	(147-159)	(145-157)	(0.68-0.76)
Heart failure	281	307	271	261	262	266	308	321	305	1.08
	(272-290)	298-316)	(262-280)	(253-270)	(253-270)	(257-274)	(299-316)	(312-330)	(296-313)	(1.04-1.13)
COPD	**514**	**458**	**415**	**399**	**369**	**386**	**353**	**365**	**310**	**0.60**
	(502-526)	(447-469)	(404-426)	(388-409)	(359-379)	(376-396)	(343-362)	(355-374)	(301-319)	(0.58-0.63)

Table 2:Changes in mean length of hospital stay (days) in women (A) and men (B)

Table 2A

	2000	2001	2002	2003	2004	2005	2006	2007	2008	Change 2008 vs 2000 (%)	p-value for time effect
Major osteoporotic fractures	**16.1**	**15.0**	**14.6**	**13.8**	**12.9**	**12.2**	**11.5**	**11.4**	**11.0**	**-31.6%**	**<0.001**
Hip fractures	19.0	17.8	17.9	17.6	16.5	16.0	14.9	14.7	14.0	-26.5%	<0.001
Non-hip fractures	12.4	11.5	11.0	9.9	9.4	8.8	8.7	8.6	8.5	-32.1%	<0.001
Spine fractures	*16.7*	*14.8*	*16.7*	*15.6*	*13.9*	*13.4*	*13.4*	*12.3*	*12.6*	*-24.5%*	*<0.001*
Distal radius fractures	*8.7*	*8.3*	*7.0*	*6.2*	*6.3*	*5.7*	*5.5*	*5.6*	*5.4*	*-38.3%*	*<0.001*
Proximal humerus fractures	*15.0*	*14.2*	*13.2*	*12.4*	*11.6*	*11.5*	*11.3*	*10.9*	*10.5*	*-30.1%*	*<0.001*
Major CV events	**17.3**	**16.1**	**15.4**	**15.2**	**14.6**	**13.4**	**12.7**	**12.0**	**11.0**	**-36.1%**	**<0.001**
Acute MI	12.6	12.1	11.9	11.2	10.2	9.6	9.4	9.3	9.5	-24.1%	<0.001
Stroke	23.7	21.6	20.7	20.7	19.8	18.2	16.7	14.8	10.7	-55.1%	<0.001
Heart failure	16.4	15.6	15.2	15.0	15.0	13.8	13.4	13.1	12.7	-22.2%	0.006
COPD	**17.5**	**16.8**	**16.8**	**15.3**	**14.7**	**13.6**	**13.8**	**13.3**	**13.3**	**-23.9%**	**<0.001**
Breast carcinoma	**9.7**	**9.2**	**8.9**	**8.7**	**8.2**	**7.7**	**7.7**	**7.6**	**7.6**	**-21.9%**	**<0.001**

Table 2B

	2000	2001	2002	2003	2004	2005	2006	2007	2008	Change 2008 vs 2000 (%)	P value for time effect
Major osteoporotic fractures	**15.3**	**14.0**	**13.9**	**13.3**	**12.5**	**11.5**	**11.7**	**11.2**	**11.2**	**-27.1%**	**<0.001**
Hip fractures	18.8	17.2	17.4	16.7	15.9	15.2	15.1	14.4	13.8	-27.0%	<0.001
Non-hip fractures	11.1	10.5	10.0	9.7	9.2	8.3	8.6	8.4	8.6	-22.1%	<0.001
Spine fractures	*13.9*	*13.5*	*13.7*	*12.3*	*11.5*	*10.5*	*11.3*	*10.3*	*11.0*	*-20.9%*	*<0.001*
Distal radius fractures	*6.0*	*6.1*	*5.5*	*5.7*	*5.3*	*5.3*	*5.0*	*4.8*	*5.3*	*-12.0%*	*0.184*
Proximal humerus fractures	*12.4*	*11.1*	*10.4*	*11.1*	*10.4*	*9.2*	*9.6*	*10.0*	*9.6*	*-23.1%*	*0.004*
Major CV events	**13.8**	**13.1**	**12.0**	**11.7**	**11.4**	**10.5**	**10.2**	**9.8**	**9.7**	**-30.1%**	**<0.001**
Acute MI	9.4	9.3	8.6	8.2	8.0	7.5	7.4	7.3	7.5	-19.8%	<0.001
Stroke	23.0	20.8	19.2	18.6	18.1	15.6	15.3	13.7	13.5	-41.3%	<0.001
Heart failure	14.3	13.9	12.9	12.7	12.6	12.2	12.0	11.9	11.7	-17.7%	0.225
COPD	**15.7**	**15.7**	**14.4**	**14.4**	**13.6**	**12.9**	**13.0**	**12.5**	**12.3**	**-21.6%**	**<0.001**

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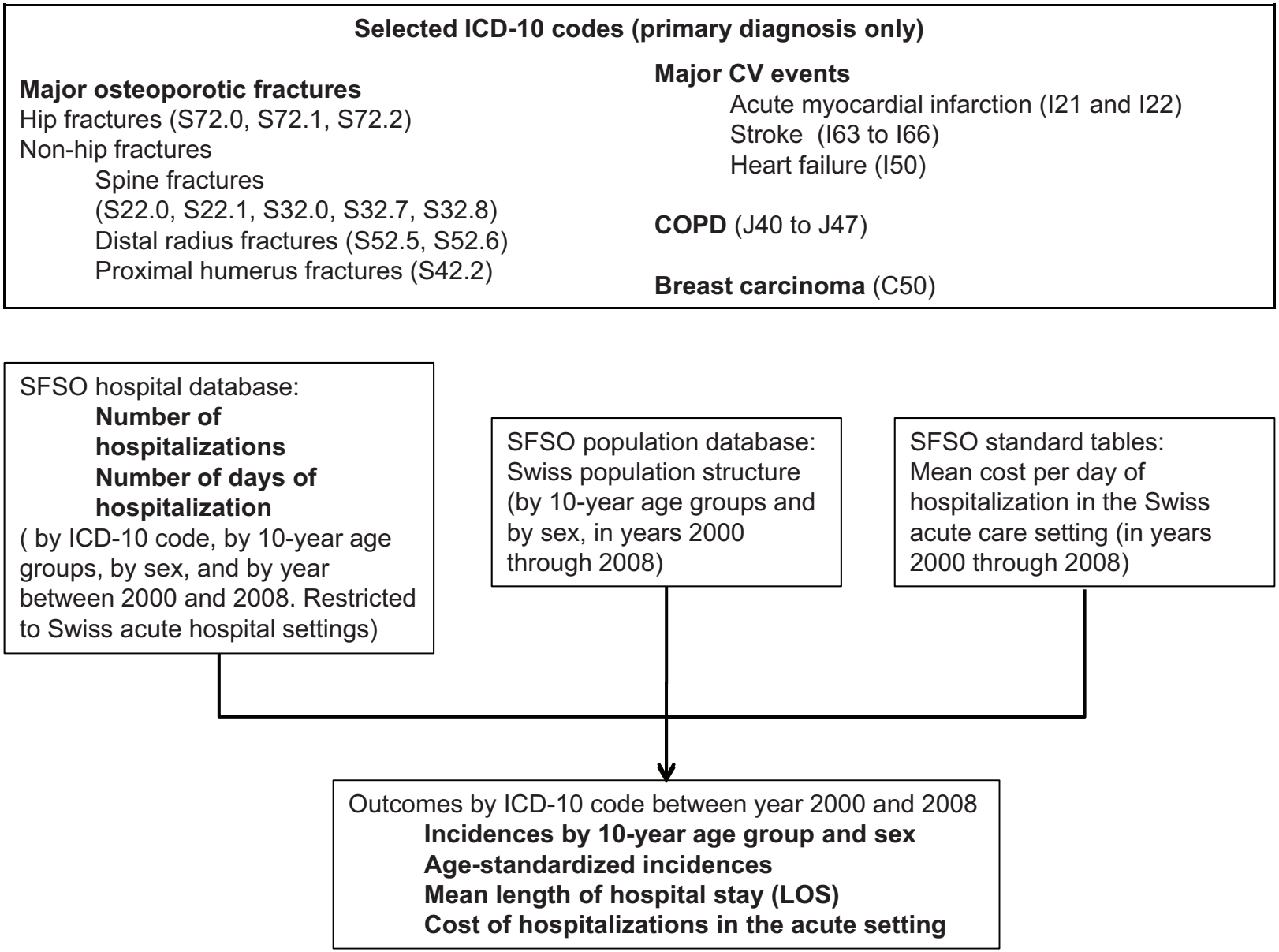
Figure 1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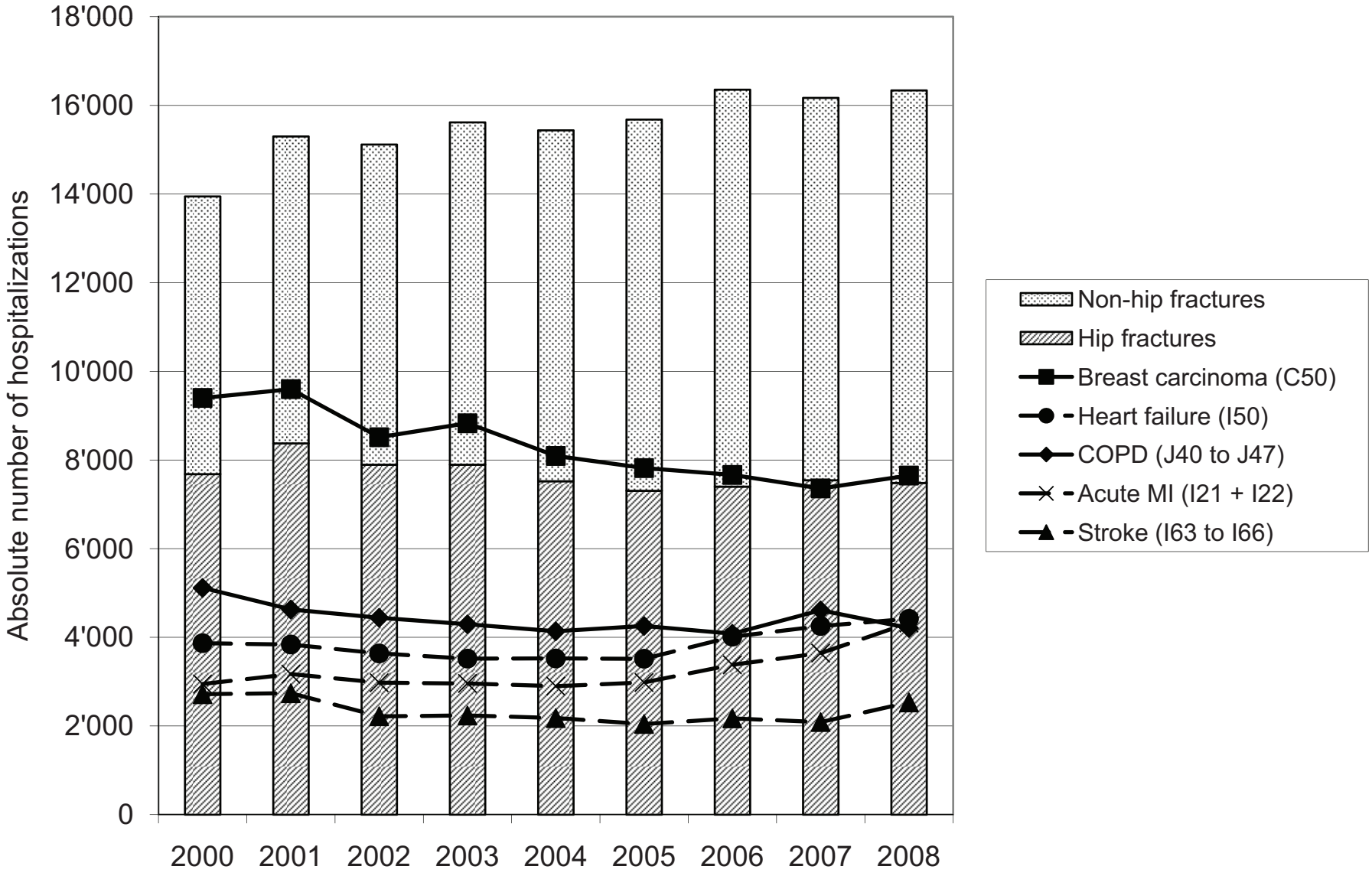
Non-hip fractures
Spine fractures
(S22.0, S22.1, S32.0, S32.7, S32.8)
Distal radius fractures (S52.5, S52.6)
Proximal humerus fractures (S42.2)
Major CV events
Acute myocardial infarction (I21 and I22)
Stroke (I63 to I66)
Heart failure (I50)
COPD (J40 to J47)
Breast carcinoma (C50)
SFSO hospital database:
Number of hospitalizations
Number of days of hospitalization
(by ICD-10 code, by 10-year age groups, by sex, and by year between 2000 and 2008. Restricted to Swiss acute hospital settings)
SFSO population database: Swiss population structure (by 10-year age groups and by sex, in years 2000 through 2008)
SFSO standard tables: Mean cost per day of hospitalization in the Swiss acute care setting (in years 2000 through 2008)
Outcomes by ICD-10 code between year 2000 and 2008
Incidences by 10-year age group and sex
Age-standardized incidences
Mean length of hospital stay (LOS)
Cost of hospitalizations in the acute setting

Figure 2A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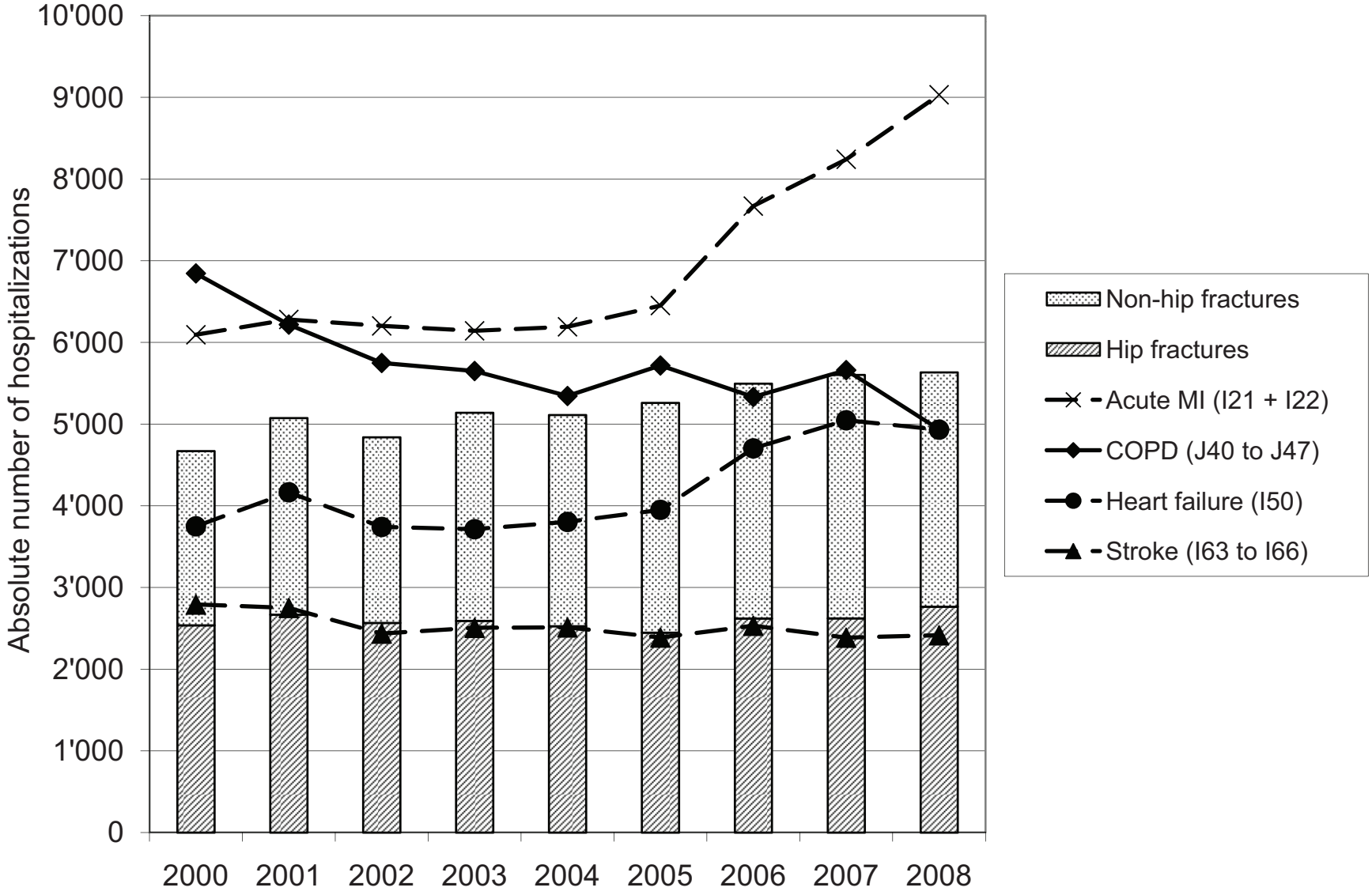
16'000
14'000
12'000
10'000
8'000
6'000
4'000
2'000
0
Absolute number of hospitalizations
2000
2001
2002
2003
2004
2005
2006
2007
2008
Non-hip fractures
Hip fractures
Breast carcinoma (C50)
Heart failure (I50)
COPD (J40 to J47)
Acute MI (I21 + I22)
Stroke (I63 to I66)

Figure 2B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9'000
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5'000
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3'000
2'000
1'000
0
Absolute number of hospitalizations
2000
2001
2002
2003
2004
2005
2006
2007
2008
Non-hip fractures
Hip fractures
Acute MI (I21 + I22)
COPD (J40 to J47)
Heart failure (I50)
Stroke (I63 to I66)

Figure 3A Women

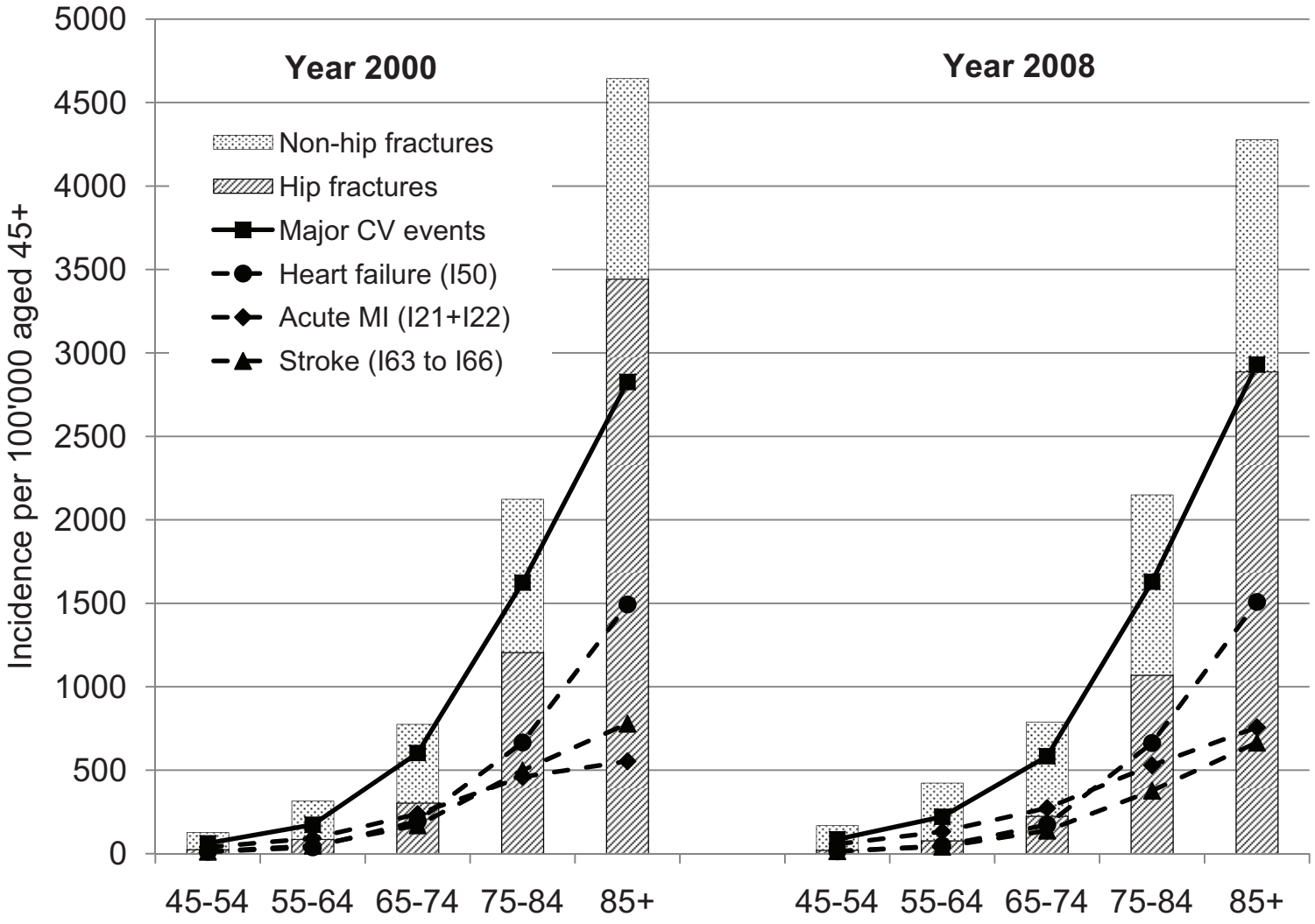


Figure 3B Men

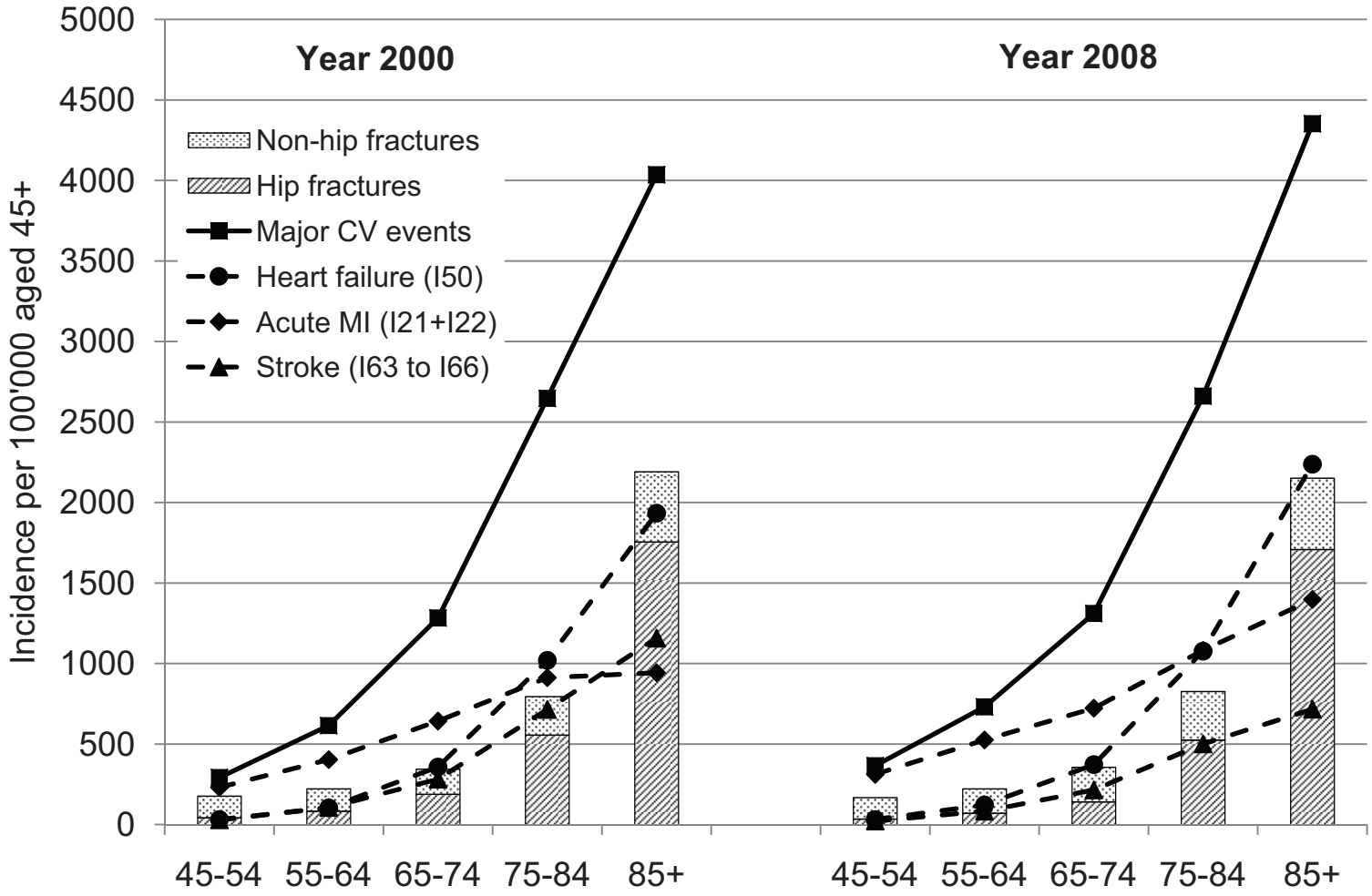
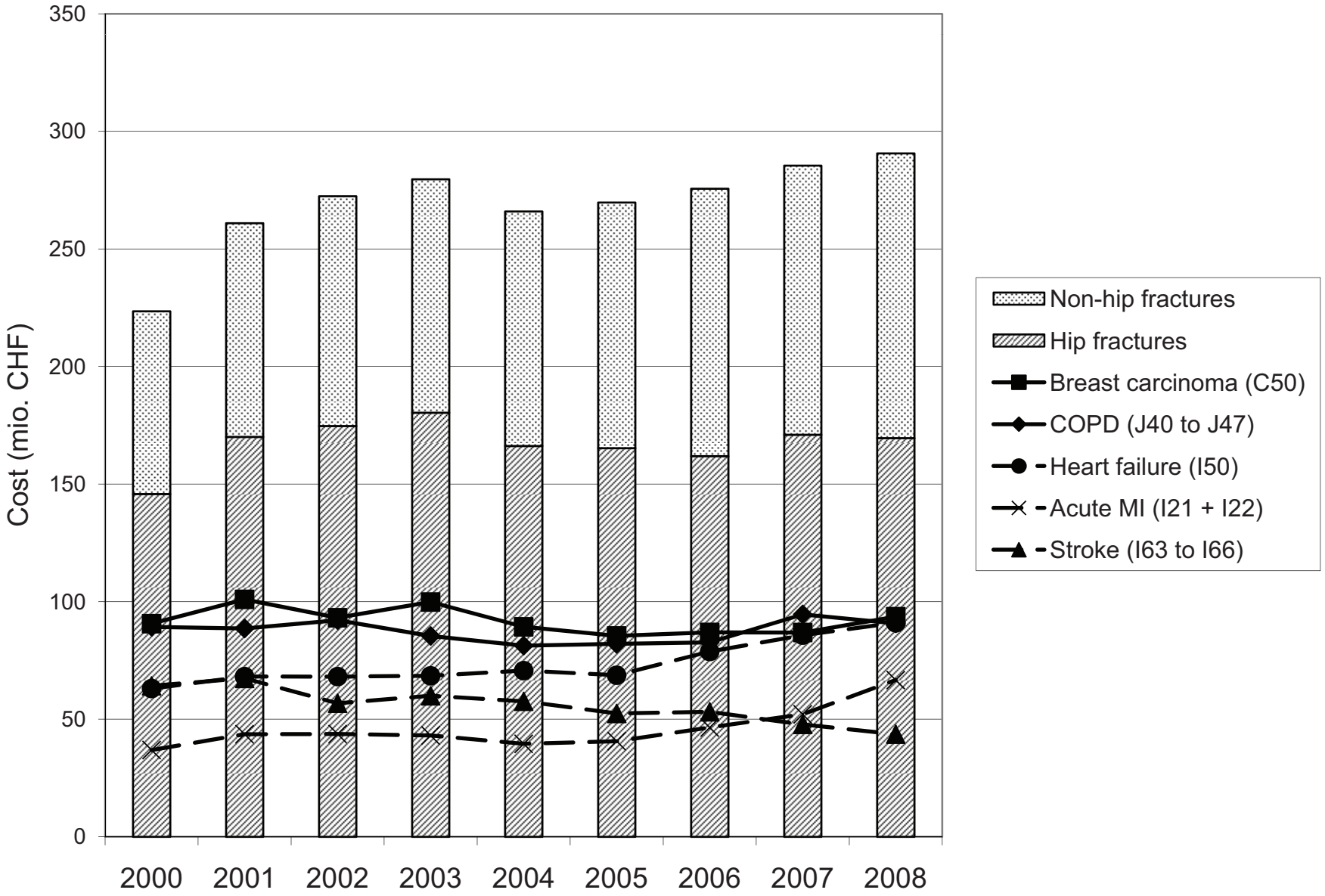


Figure 4A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300
250
200
150
100
50
0
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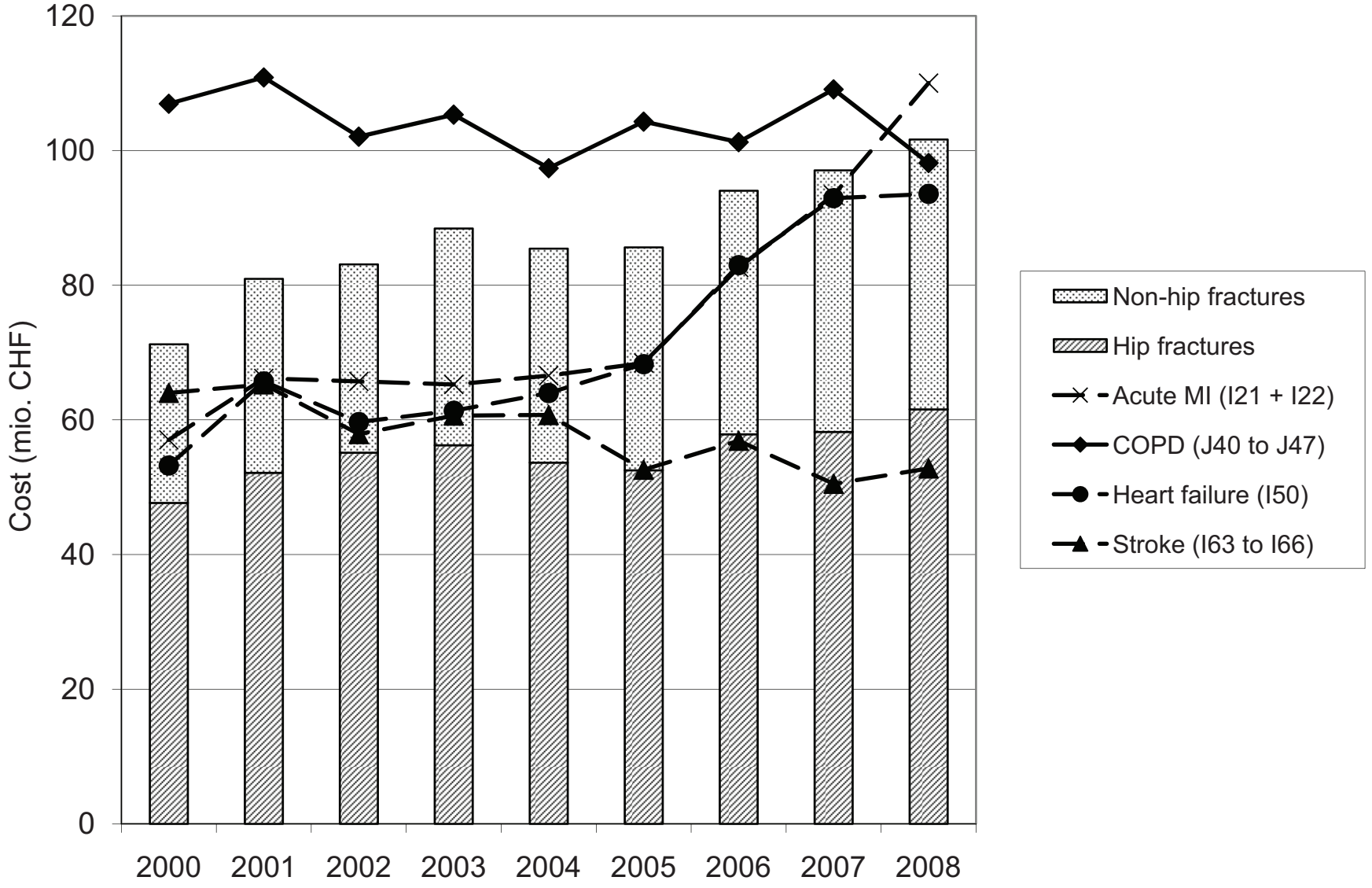
2000
2001
2002
2003
2004
2005
2006
2007
2008
Non-hip fractures
Hip fractures
Breast carcinoma (C50)
COPD (J40 to J47)
Heart failure (I50)
Acute MI (I21 + I22)
Stroke (I63 to I66)

Figure 4B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Cost (mio. CHF)
2000
2001
2002
2003
2004
2005
2006
2007
2008
Non-hip fractures
Hip fractures
Acute MI (I21 + I22)
COPD (J40 to J47)
Heart failure (I50)
Stroke (I63 to I66)

Figure 5A

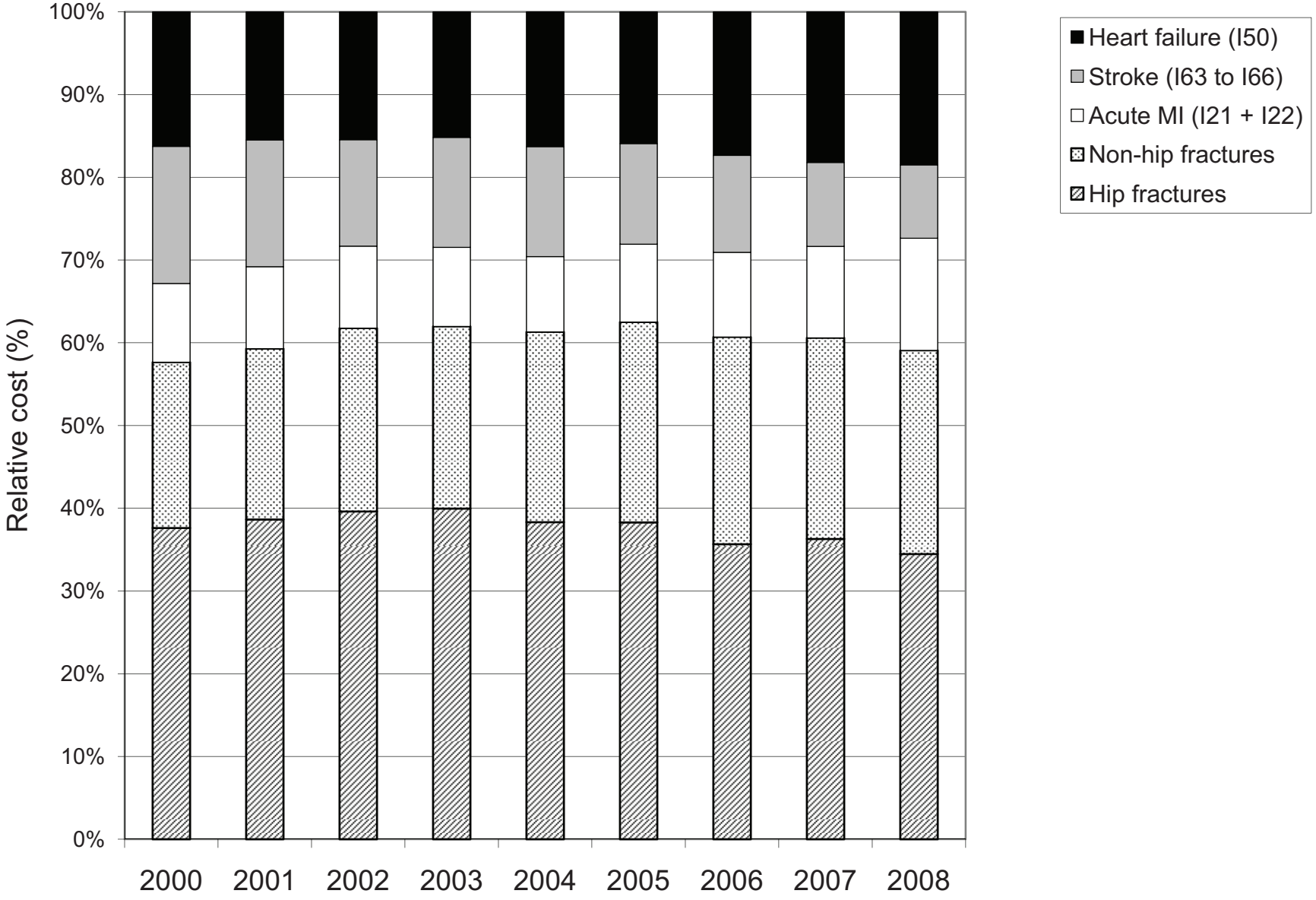
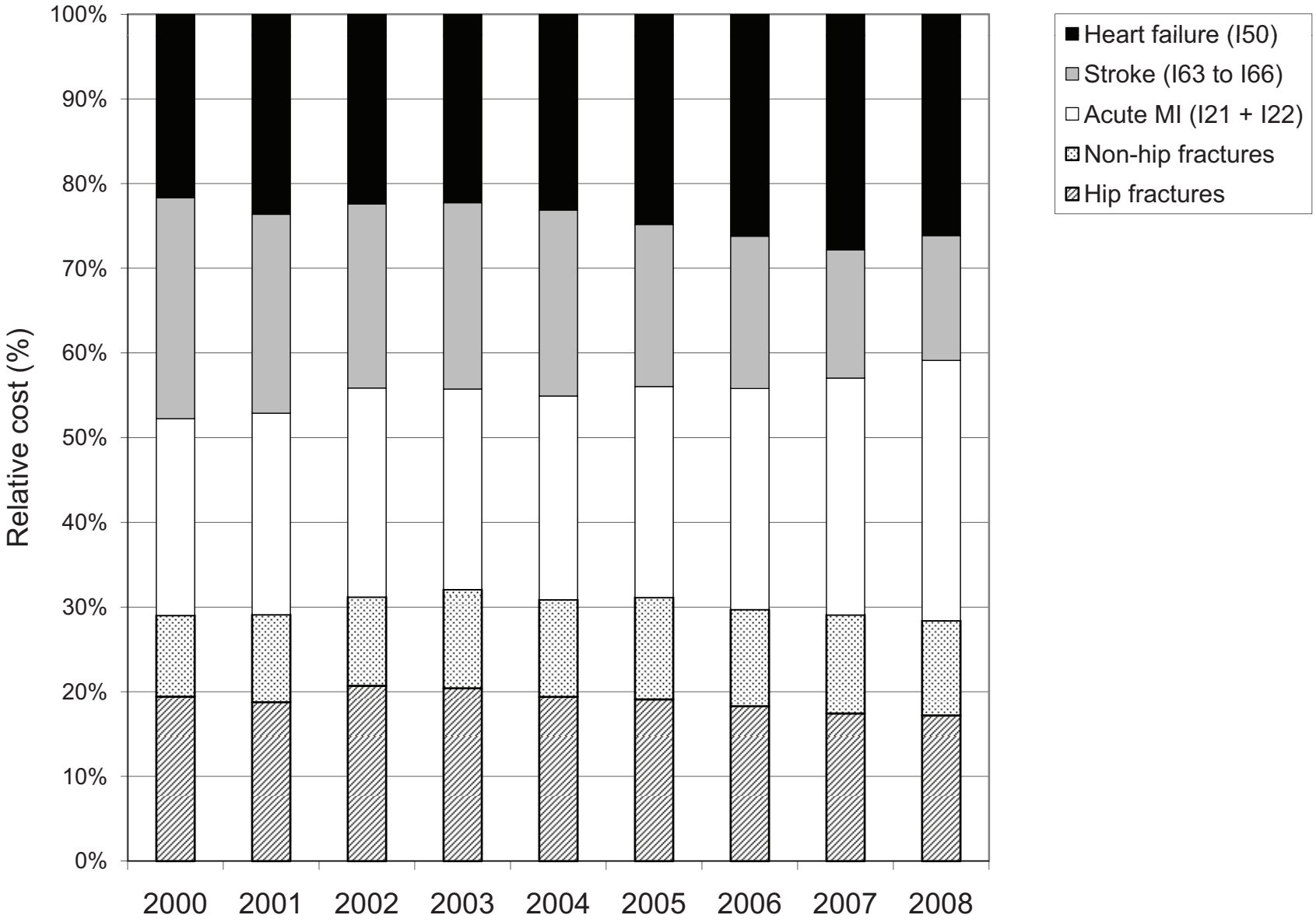

100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Relative cost (%)
2000
2001
2002
2003
2004
2005
2006
2007
2008
Heart failure (I50)
Stroke (I63 to I66)
Acute MI (I21 + I22)
Non-hip fractures
Hip fractures

Figure 5B


100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Relative cost (%)
2000
2001
2002
2003
2004
2005
2006
2007
2008
Heart failure (I50)
Stroke (I63 to I66)
Acute MI (I21 + I22)
Non-hip fractures
Hip fractures